CHAPTER 44

Generalized Weakness

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This chapter focuses on selected causes of generalized weakness. Although many causes of weakness exist, the differential diagnosis will be considerably narrowed if care is taken to differentiate between weakness and fatigue or asthenia. Fatigue is the inability to continue performing a task following multiple repetitions. A sense of weariness or exhaustion without demonstrated muscle weakness is asthenia. Asthenia may lead to muscle weakness over time because of deconditioning. True weakness is the inability to perform the first repetition of a task.

Symptoms of weakness can be seen in a wide variety of conditions. These include infectious, neurologic, and genetic problems.

AMYOTROPHIC LATERAL SCLEROSIS

Also known as Lou Gehrig's disease, amyotrophic lateral sclerosis (ALS) is a progressive neuromuscular condition that affects about 30,000 people in the United States. The disease is most commonly seen in men between 30 and 60. Patients become severely disabled over a period of months to years with death occurring typically within 5 years of diagnosis.

Symptoms

- Dysphagia
- Dysarthria
- Muscle weakness in limbs and bulbar muscles ++++

Signs

- Asymmetric muscle weakness
- Hyperreflexia
- Fasciculations
- Muscle atrophy ++++
- Normal sensory examination
- Normal mental status

Workup

- The clinical diagnosis of ALS is characterized by a combination of both upper and lower motor neuron lesions, with evidence of progression and the absence of an alternative diagnosis.

- Nerve conduction studies and electromyography may be performed.
- Neuroimaging and blood and cerebrospinal studies may be helpful to exclude alternative diagnoses.

Comments and Treatment Considerations

Management involves aggressive relief of symptoms and prevention of complications such as aspiration pneumonia, spasticity, and contractures. The only agent currently considered for treatment is riluzole, 50 mg orally twice daily. Riluzole reduces release of presynaptic glutamate and may slow progression. Muscle spasticity may improve with use of baclofen or diazepam. Depression is common in ALS and should be treated appropriately. Supportive care is essential and may include the coordination of multiple services including physical therapy, speech therapy, occupational therapy, speech pathology, and nutrition.

BOTULISM

Diagnosis is based on a history of recent ingestion of home-canned, smoked, or reheated foods and demonstration of toxin in serum or food. In infants younger than 1 year, botulism may be associated with the consumption of honey.

Symptoms

- Diplopia
- Dry mouth
- Dysphagia
- Dysphonia
- Muscle weakness

Signs

- Loss of accommodation
- Ptosis, cranial nerve palsies
- Impairment of extraocular muscles
- Fixed, dilated pupils
- Normal sensory examination
- Normal mental status examination
- Constipation

Workup

- In the acute setting, diagnosis is most commonly clinical.
- EMG testing may be helpful in supporting the diagnosis.
- Botulinum toxin present in patient's serum or stool

Comments and Treatment Considerations

Rapid identification and treatment are essential because of the high fatality rate associated with respiratory paralysis. In foodborne botulism, enemas or cathartics may be helpful. In wound botulism, debridement and antimicrobial therapy should be considered. All cases should be reported to the local public health authorities.

The CDC should be contacted immediately when botulism is suspected for assistance with obtaining antitoxin and assays for identification of toxin. Because botulinum toxin is destroyed at high temperatures, home-canned foods should be boiled during preparation.

CEREBROVASCULAR ACCIDENT/TRANSIENT ISCHEMIC ATTACK

CVA or acute stroke is a sudden neurologic deficit caused by vascular compromise in the brain. Strokes are ischemic as the result of a thrombotic, embolic, or hemorrhagic occlusion. If neurologic symptoms resolve spontaneously within 24 hours, the diagnosis of TIA is appropriate.

Symptoms
- Weakness or paralysis +++
- Dysarthria
- Visual change
- Loss of consciousness
- Headache
- Seizure

Signs
- Paralysis or paresis
- Upper motor neuron lesion
- Hemianopsia or other defined visual finding
- Nystagmus

Workup
- Head CT differentiates between ischemic and hemorrhagic stroke.
- MRI and MRA may be helpful if available.
- Obtain ECG, chest x-ray, CBC, renal function, PT/INR, and serum electrolytes.
- Other tests may include carotid Doppler studies and echocardiogram.

Comments and Treatment Considerations
Initial management includes stabilization and evaluation for potential complications. Medical therapy, including antiplatelet therapy, should begin as soon as possible after imaging studies. Hyperglycemia, fever, and hypertension are associated with poor prognosis. Hypertension should be treated cautiously to prevent the risk of reducing cerebral perfusion. In selected patients presenting within 3 hours of symptom onset, thrombolysis may be appropriate (see Chapter 19 for more information).

GUILLAIN-BARRÉ SYNDROME

Patients present with an acute, progressive radiculoneuropathy resulting in ascending, symmetric weakness. The condition often ensues following an acute infection, surgical procedures, or

immunizations. An association with the syndrome is sometimes seen with *Campylobacter jejuni* gastroenteritis.

Symptoms
- Weakness of variable severity ++++
- Proximal, symmetric symptoms
- Dysphagia
- Numbness and tingling
- Palpitations
- Flushing
- Encopresis due to loss of sphincter control

Signs
- Tachycardia
- Cardiac dysrhythmias
- Hypotension or hypertension
- Absent or depressed deep tendon reflexes

Workup
- CSF demonstrates a normal cell content and high protein concentration.
- Nerve conduction studies and needle electromyography are helpful in making the diagnosis.

Comments and Treatment Considerations
Several variant forms of Guillain-Barré syndrome exist. Up to 30% of patients require intubation and ventilatory support. Vital capacity and negative inspiratory force should be measured regularly. Patients may not be able to clear secretions or swallow. Dysautonomia may require management with pressors, fluids, and other agents. IVIg and plasma exchange are equivalent in efficacy. Most patients eventually recover over a period of several months; 10% to 20% have some residual deficit.

MULTIPLE SCLEROSIS

Multiple sclerosis is one of the most common neurologic causes of muscle weakness. About 300,000 patients are affected in the United States with the highest incidence in young adults between 20 and 40 years of age and a twofold predominance in women. The disease is thought to have an autoimmune basis.

Symptoms
- Numbness or tingling in a limb
- Gait disorder
- Lower or upper extremity weakness
- Diplopia
- Urinary urgency or hesitancy
- Sudden loss of vision or blurring in one eye

Signs
- Absent abdominal reflexes
- Hyperreflexia
- Lower extremity ataxia
- Impaired vibratory sensation
- Impaired rapid alternating movements
- Nystagmus
- Intention tremor
- Spasticity
- Dysarthria
- Impaired pain or temperature sensation

Workup
- Diagnosis is based on symptomatology as well as laboratory and imaging. Cases are classified as "possible MS, MS, or not MS" based on the McDonald criteria.
- CSF shows slightly increased protein, mild lymphocytosis, and positive oligoclonal bands.
- MRI of the brain and cervical spinal cord may demonstrate multiple white matter lesions.
- Evoked potential testing may provide further diagnostic information.

Comments and Treatment Considerations
Partial recovery from acute episodes is common but predicting relapse is difficult. High-dose prednisone, 60 to 80 mg/day, for 1 week hastens recovery from acute episodes but will not provide long-term benefit or prevent relapse. Incomplete remissions eventually lead to spasticity, ataxia, impaired vision, and urinary incontinence. Relapses are more common in the first months following pregnancy.

In patients with progressive disease, daily injections of glatiramer acetate may reduce frequency of exacerbations. Cyclophosphamide, azathioprine, methotrexate, cladribine, and mitoxantrone have been used with variable success in delaying secondary symptoms. During acute episodes, excessive fatigue should be avoided. Although disability is likely to eventually occur, up to half of all patients are without significant permanent disability even 10 years after onset of symptoms.

MUSCULAR DYSTROPHY

The muscular dystrophies are an inherited group of disorders causing progressive muscle weakness and wasting. The inheritance pattern, age of onset, muscle pattern distribution, and prognosis are variable depending on the specific dystrophy (Table 44-1). Patients may also have accompanying skeletal deformities and contractures.

Workup
- Serum creatinine kinase may be elevated, especially in Duchenne and Becker dystrophies.

Table 44-1. Signs and Symptoms of the Muscular Dystrophies

DISORDER	INHERITANCE	AGE AT ONSET	DISTRIBUTION OF WEAKNESS	PROGNOSIS
Duchenne	X-lined recessive	1-5 years	Pelvic, shoulder girdle then limb and respiratory muscles	Rapid; death within 5 years of onset
Becker	X-lined recessive	2-25 years	Pelvic, shoulder girdle	Slow; may have normal life expectancy
Erb	Autosomal recessive	10-30 years	Pelvic, shoulder girdle	Variable; severe disability in mid to later life
Fascioscapulohumeral	Autosomal dominant	Any	Face and shoulder, later pelvis and legs	Slow; usually normal life expectancy
Emery-Dreifuss	X-linked recessive or autosomal dominant	5-10 years	Humeroperoneal or scapuloperoneal	Variable
Ocular	Autosomal dominant	5-30 years	External ocular muscles; some mild weakness of arms, neck, and face	Slow

- EMG may confirm myopathic weakness.
- Genetic carrier detection is an important component of the evaluation of patients and their families.

Comments and Treatment Considerations

No specific treatments are recommended for the muscular dystrophies. Contractures and deformities are worsened by bed rest, so patients and their families should be encouraged to lead as normal a life as possible. Physical therapy and orthotics may be helpful in preventing disuse sequelae.

MYASTHENIA GRAVIS

In myasthenia gravis autoantibodies bind to the acetylcholine receptors of the neuromuscular junction resulting in fluctuating weakness and fatigability of voluntary muscles. This condition may be fatal when respiratory muscles are affected. Symptoms may occur at all ages and can be associated with thymic tumors, thyrotoxicosis, SLE, or RA. Exacerbations may occur with the use of anesthesia, sedatives, or narcotics.

Symptoms

- Diplopia
- Ptosis
- Dysphagia
- Fluctuating weakness ++++

Signs

- Cranial nerve palsies
- Normal papillary responses
- Muscle weakness increases with sustained activity and improves with rest. +++
- Normal sensation ++++
- Preserved deep tendon reflexes

Workup

- Elevated serum acetylcholine receptor antibodies
- Chest CT to determine presence of thymoma
- Edrophonium challenge with a dose of 2 mg, IV, initially followed by 8 mg about 30 seconds later if tolerated. Improvement typically lasts about 5 minutes.
- EMG studies indicate a disturbance of neuromuscular transmission.

Comments and Treatment Considerations

Anticholinesterase medications such as neostigmine and pyridostigmine provide symptomatic relief but do not alter the course of the disease. Immunomodulating agents, such as corticosteroids, azathioprine, and cyclosporine may be used. Plasma exchange or IVIg therapy are often considered as "bridge" therapy. Thymectomy should be considered in all patients younger than age 60. Spontaneous remissions can occur.

POLIOMYELITIS

Poliomyelitis (polio) is caused by an enteroviral infection of the lower motor neurons. Infection occurs predominantly by the fecal-oral route. Although rare in the developed world, polio remains common across the globe and has been targeted for eradication by the World Health Organization. Prevention is effective with the use of a parenteral inactive vaccine in children.

Symptoms
- Headache
- Sore throat
- Stiff neck
- Abdominal pain
- Weakness ++++

Signs
- Fever
- Muscle pain and spasm
- Meningismus
- Lower motor neuron paresis or paralysis, commonly asymmetric

Workup
- CSF reveals lymphocytosis.
- Viral culture, serum titers

Comments and Treatment Considerations
Treatment is mainly supportive. For every 1 person with paralytic polio, an estimated 200 subclinical cases exist; 15% to 30% of adults who contract paralytic polio die from the illness.

RABIES

Rabies is caused by a rhabdovirus infection transmitted to humans by bites from animals with infected saliva. Although cases are rare in the United States, the most common vectors are bats, raccoons, skunks, foxes, and coyotes. Prevention includes immunization of household cats and dogs and avoidance of animals associated with rabies.

Symptoms
- Pain at the site of the animal bite
- Fever
- Nausea
- Headache
- Muscle weakness and confusion
- Hydrophobia

Signs
- Delirium
- Painful laryngeal spasms

- Paresis
- Coma

Workup

- Diagnosis is confirmed by fluorescent antibody testing of the animal's brain.
- The risk of infection must be carefully evaluated based on the type of exposure, circumstances surrounding exposure, and the evidence of a bite.
- Consultation with the local or state health department may be necessary to determine the need for prophylaxis.

Comments and Treatment Considerations

In previously unvaccinated patients exposed to rabies, rabies immune globulin (RIg) is administered once to provide immediate antibodies. Postexposure prophylaxis after contact with bats may be appropriate even if a bite, scratch, or mucous membrane exposure is not obvious because data suggest bats can transfer the virus through minor or unrecognized bites. All wounds should be thoroughly cleansed with soap and water and irrigated with an agent such as povidone-iodine solution. As much RIg as possible should be administered at 20 IU/kg by infiltrating around the wound. Any remaining volume can be given IM at a site distant from vaccine administration. Rabies vaccine 1 mL, IM, should be given in the deltoid area on days 0, 3, 14, and 28 after exposure in previously unvaccinated patients. Rabies vaccine 1 mL IM should be given in the deltoid area on days 0 and 3 for patients previously vaccinated. The rabies vaccine should not be given in the gluteal region because of resulting lower neutralizing antibody titers.

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